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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,142	06/26/2001	Hirobumi Aoki	Q64574	1209

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/869,142

Applicant(s)

AOKI ET AL.

Examiner

Christian L. Fronda

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8, 10, 11 and 60-72 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 11 is/are allowed.
- 6) ☒ Claim(s) 8, 10, 60-72 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 01/10/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

1. The finality of the previous Office Action dated 09/09/2004 has been withdrawn in view of new rejections and new grounds for rejection stated in the instant Office Action.
2. Previously withdrawn claims 62-71 cited in the previous Office Action dated 09/09/2004 have been rejoined and examined with the elected claims 8, 10, 11, 60, 61, and 72.
3. Claims 8, 10, 11, and 60-72 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. Claims 8, 10, 60-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed 01/10/2005 have been considered but are not persuasive. Applicants' argue that applicants had possession of the claimed invention by describing distinguishing characteristics of the claimed microorganism, providing a reduction to practice of *Rhodococcus* sp. SD826, and describing various *Rhodococcus* strains known in the art and their endogenous activities. Applicants conclude that there is no requirement that the claimed microorganisms be described by their genetic information. The Examiner respectfully disagrees for reasons of record as supplemented below.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001, which states:

"Eli Lilly explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of compounds is claimed. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that

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distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed.” (see p. 1100, 1st column, line 47 to 2nd column, line 2).

While the examiner acknowledges that the microbes have been characterized based on their enzymatic properties, a review of the claims and the specification indicates that the enzyme/proteins having the “activity of converting a cyano group into a carboxyl group” and the “activity of converting a cyano group into an amide group” as recited are important and critical to the claimed invention. The specification refers to the claimed invention as encompassing variant microorganisms having destroyed or deleted enzymes or destroyed or deleted enzyme factors participating in the production of amide compounds:

“For example, the variant microorganism strain reduced or defective in the ability to produce amide compounds applied to the present invention may be acquired by destroying or deleting enzymes or factors regulating the enzymes participating in the production of amide compounds and regions of gene encoding these using genetic engineering techniques. More specifically, it is realized as follows. Related genes of enzymes contributing to the reaction are isolated and analyzed, a gene fragment having incorporated therein is introduced, a sequence having homology to the base sequence is introduced into a microorganism, and homologous recombination between enzyme-related genes on the chromosome is induced to cause insertion or deletion of the base sequence.” (see specification on p. 22, lines 3-12).

The claims are genus claims encompassing a genus of nitrilases of any amino acid sequence and structure which converts any cyano group on any molecule into any carboxyl group and a genus of nitrile hydratases of any amino acid sequence and structure which converts any cyano group on any molecule into any amide group. The scope of the each genus includes many enzymes with widely differing structural, chemical, and physical characteristics. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exists.

While Examples 11-19 of the specification describes *Rhodococcus* microorganisms having an overexpression of nitrilase, nitrile hydratase, and amidase (SEQ ID NOs: 2, 4, 5, and 7); the

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recitation of the activities performed by the nitrilases and nitrile hydratases does not define any structural features commonly possessed by nitrilases and nitrile hydratases. Furthermore, the specification does not describe and define any structural features commonly possessed by each enzyme. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each claimed genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of genus of nitrilases of any amino acid sequence and structure which converts any cyano group on any molecule into any carboxyl group and a genus of nitrile hydratases of any amino acid sequence and structure which converts any cyano group on any molecule into any amide group.

Amending the claims to recite the specific encoding nucleotide sequence and amino acid sequence of the nitrilase, nitrile hydratase, and amidase (SEQ ID NOs: 2, 4, 5, and 7) may overcome the rejection.

Claim Rejections - 35 U.S.C. § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the

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manner in which the invention was made.

6. Claims 8, 10, 60-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 4,629,700 (Prevatt et al.) in view of the combined teachings of Alberts et al. (Molecular Biology of the Cell. 3rd ed. New York: Garland Publishing, Inc.; 1994. pp. 325-326) and Bunch (Antonie Van Leeuwenhoek. 1998 Jul-Oct;74(1-3):89-97)

US Patent 4,629,700 teaches the bacterial strain *Rhodococcus* sp. ATCC39484 and a process comprising culturing said bacterial strain *Rhodococcus* sp. ATCC39484 at 32°C in the presence of nitriles for the purposed of producing compounds from nitriles (see entire patent , claims, and examples).

JP2001069978 provides evidence that *Rhodococcus* sp. ATCC39484 inherently has an endogenous nitrile hydratase which converts nitriles to amides and has excellent position selectivity to an aromatic polynitrile (see abstract; publication used as evidentiary reference).

Stevenson et al. (Biotechnol Appl Biochem. 1992 Jun;15(3):283-302) provide evidence that *Rhodococcus* sp. ATCC39484 inherently has an endogenous nitrilase which converts nitriles to carboxylic acids (see abstract; publication used as evidentiary reference).

The teachings of US Patent 4,629,700 differ from the claims in that the taught *Rhodococcus* sp. ATCC39484 is not defective or reduced in the endogenous activity of converting a cyano group into an amide, which is performed by the action of a nitrile hydratase.

Alberts et al. teaches that in bacteria normal genes can be replaced with mutant genes by homologous recombination (see pp. 325-326 and Figure 7-42).

Bunch teach that *Rhodococci* have been shown to convert nitriles to amides or carboxylic acids, and that the two main types of enzymes involved in nitrile biotransformations are a nitrile hydratase for amide synthesis and a nitrilases for carboxylic acid synthesis with no amide intermediate released (see entire publication). Furthermore, Bunch teach that rhodococcal nitrilases are capable of hydrolyzing a wide range of nitriles, often with region- and stereoselectivity (see pp. 94-96).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the *Rhodococcus* sp. ATCC39484 such that its endogenous nitrile hydratase gene is replaced with a mutant endogenous gene encoding an endogenous mutant nitrile hydratase having defective or reduced activity as taught by Alberts et al. Thus, the resulting mutant strain of said *Rhodococcus* sp. ATCC39484 has an endogenous nitrilase, which converts cyano groups to

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carboxyl groups, and has an endogenous nitrile hydratase having defective or reduced activity of converting a cyano group into an amide. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of creating beneficial mutant *Rhodococcus* strains that produce carboxylic acids without making amide intermediates.

Claim 63 which recites a method for making is obvious since one of ordinary skill in the art at the time the invention was made would perform the recited steps of mutating *Rhodococcus* sp. ATCC39484 and screening for the purposes of obtaining the claimed mutant strain of said *Rhodococcus* sp. ATCC39484 that has an endogenous nitrilase and has an endogenous mutant nitrile hydratase having defective or reduced activity.

The mutant strain of said *Rhodococcus* sp. ATCC39484 stated above having an endogenous nitrilase and an endogenous mutant nitrile hydratase having defective or reduced activity inherently has the activity of converting each of the nitrile compounds recited in claims 64, 66, 67, 68 since rhodococcal nitrilases are capable of hydrolyzing a wide range of nitriles, often with region- and stereoselectivity as taught by Bunch. Furthermore, the mutant strain of said *Rhodococcus* sp. ATCC39484 inherently has the activity of making the amide of claim 65 since JP2001069978 provides evidence that the nitrile hydratase of *Rhodococcus* sp. ATCC39484 converts nitriles to amides and has excellent position selectivity to an aromatic polynitrile.

In regard to claim 69, the mutant strain of said *Rhodococcus* sp. ATCC39484 stated above having an endogenous nitrilase and an endogenous mutant nitrile hydratase having defective or reduced activity inherently would produce by products from a nitrile compound in an amount that is 0.5 mol% or less of total amount of carboxylic acid because the nitrile hydratase has defective or reduced activity

Claims 60-62 and 70 are product by process claims which recite limitations for making the claimed microorganism. MPEP §2113 states:

“[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

In view of this, claims 62 and 70 are not limited to the process steps and the recited

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mutagens used to make the claimed microorganism. Thus, the claims 62 and 70 are obvious over mutant strain of said *Rhodococcus* sp. ATCC39484 stated above having an endogenous nitrilase and an endogenous mutant nitrile hydratase having defective or reduced activity.

In regard to claims 71 and 72 it would have been obvious to culture at 32°C and in the presence of nitriles (as taught by US Patent 4,629,700) the mutant strain of said *Rhodococcus* sp. ATCC39484 stated above having an endogenous nitrilase and an endogenous mutant nitrile hydratase having defective or reduced activity for the purposes of producing carboxylic acids and amides from nitriles.

Thus, the claims are within the ordinary skill in the art to make and use at the time the invention was made, and was as a whole clearly *prima facie* obvious.

Amending the claims to recite the specific encoding nucleotide sequence and amino acid sequence of the nitrilase, nitrile hydratase, and amidase (SEQ ID NOs: 2, 4, 5, and 7) may overcome the rejection.

Conclusion

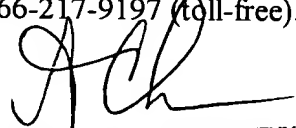
7. Claim 11 is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (571)272-0929. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571)272-0928. The official fax phone number (703)872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (571)272-1600.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

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